



FDA Drug Safety Communication: FDA requires label changes to warn of risk for possibly permanent nerve damage from antibacterial fluoroquinolone drugs taken by mouth or by injection

Safety Announcement

[8-15-2013] The U.S. Food and Drug Administration (FDA) has required the drug labels and Medication Guides for all fluoroquinolone antibacterial drugs be updated to better describe the serious side effect of peripheral neuropathy. This serious nerve damage potentially caused by fluoroquinolones (see Table for a list) may occur soon after these drugs are taken and may be permanent.

The risk of peripheral neuropathy occurs only with fluoroquinolones that are taken by mouth or by injection. Approved fluoroquinolone drugs include levofloxacin (Levaquin), ciprofloxacin (Cipro), moxifloxacin (Avelox), norfloxacin (Noroxin), ofloxacin (Floxin), and gemifloxacin (Factive). The topical formulations of fluoroquinolones, applied to the ears or eyes, are not known to cause this risk.

If a patient develops symptoms of peripheral neuropathy, the fluoroquinolone should be stopped, and the patient should be switched to another, non-fluoroquinolone antibacterial drug, unless the benefit of continued treatment with a fluoroquinolone outweighs the risk. Peripheral neuropathy is a nerve disorder occurring in the arms or legs. Symptoms include pain, burning, tingling, numbness, weakness, or a change in sensation to light touch, pain or temperature, or the sense of body position. It can occur at any time during treatment with fluoroquinolones and can last for months to years after the drug is stopped or be permanent. Patients using fluoroquinolones who develop any symptoms of peripheral neuropathy should tell their health care professionals right away.

FDA will continue to evaluate the safety of drugs in the fluoroquinolone class and will communicate with the public again if additional information becomes available.

Facts about the fluoroquinolone drug class

- Antibacterial drugs approved for the treatment or prevention of certain bacterial infections.
- Approximately 23.1 million unique patients received a dispensed prescription for an oral fluoroquinolone product from outpatient retail pharmacies during 2011. Patients receiving a dispensed prescription for ciprofloxacin, levofloxacin, or moxifloxacin accounted for 70%, 28%, and 9% of the total number of patients, respectively, during 2011. Gemifloxacin, ofloxacin, and norfloxacin each accounted for less than 1% of total patients during 2011.¹
- Within the hospital setting, there were approximately 3.8 million unique patients billed for an injectable fluoroquinolone product during 2011. Levofloxacin, ciprofloxacin, and moxifloxacin

accounted for 63%, 28%, and 13% of total unique patients, respectively, during 2011; hospital billing for ofloxacin was not captured.²

Additional Information for Patients

- If you are taking a fluoroquinolone drug (see Table for a list) by mouth or by injection, know that it may cause symptoms in the arms or legs such as pain, burning, tingling, numbness, weakness, or a change in sensation to light touch, pain or temperature . These symptoms can occur early in treatment and may be permanent.
- Contact your health care professional right away if you take a fluoroquinolone drug and experience any of the above symptoms; it may be necessary to stop the fluoroquinolone and take another antibacterial drug, but do not do so without first talking with your health care professional.
- Carefully read the Medication Guide that comes with your fluoroquinolone prescription.
- Discuss any questions or concerns about fluoroquinolone drugs with your health care professional.
- Report any side effects you experience to your health care professional and the FDA MedWatch program, using the information in the “Contact FDA” box at the bottom of the page.

Additional Information for Health Care Professionals

- Make sure your patients know to contact you if they develop symptoms of peripheral neuropathy.
- Make sure your patients receive the Medication Guide with every prescription.
- If the patient develops symptoms of peripheral neuropathy, the fluoroquinolone should be stopped and an alternative non-fluoroquinolone antibacterial drug should be used, unless the benefit of continued treatment with a fluoroquinolone outweighs the risk.
- Report adverse reactions involving fluoroquinolones to the FDA MedWatch program, using the information in the “Contact FDA” box at the bottom of the page.

Data Summary

Peripheral neuropathy is an identified risk of fluoroquinolones and was added to the *Warnings* or *Warnings and Precautions* sections of all the labels for systemic (oral and injectable) fluoroquinolone drugs in 2004. The risk of peripheral neuropathy is also described in the Medication Guides for these products. FDA has continued to receive reports of peripheral neuropathy even after the adverse

reaction was added to the fluoroquinolone drug labels. The results of FDA’s recent review of the Adverse Event Reporting System (AERS) database indicate that although the risk of peripheral neuropathy is described in the drug labels of each marketed systemic fluoroquinolone, the potential rapid onset and risk of permanence were not adequately described.

The recent AERS review evaluated cases of fluoroquinolone-associated peripheral neuropathy with an outcome of “disability,” reported between January 1, 2003 and August 1, 2012. The review showed a continued association between fluoroquinolones use and disabling peripheral neuropathy. However, because AERS is a spontaneous reporting system, an incidence of peripheral neuropathy, especially permanent damage among patients exposed to these medications, cannot be calculated. The onset of peripheral neuropathy after starting fluoroquinolone therapy was rapid, often within a few days. In some patients the symptoms had been ongoing for more than a year despite discontinuation of the fluoroquinolone. Several patients were continued on the fluoroquinolone drug despite the occurrence of neuropathic symptoms.

FDA has not identified any specific risk factors for the development of peripheral neuropathy. Peripheral neuropathy appeared to be unrelated to the duration of therapy or the age of the patient.

FDA has required manufacturers of systemic fluoroquinolone drugs to make revisions to the drug labels (*Warnings/Precautions* and *Warnings and Precautions* sections) and the Medication Guides. These label changes are to better characterize the risk of peripheral neuropathy associated with the class of systemic fluoroquinolones. If a patient develops symptoms of peripheral neuropathy, the fluoroquinolone should be stopped, and the patient should be treated with an alternative non-fluoroquinolone antibacterial drug, unless the benefit of continued treatment with a fluoroquinolone outweighs the risk.

Table. List of approved fluoroquinolone drug products

Generic name	Contained in Brand name
levofloxacin	Levaquin
ciprofloxacin	Cipro
moxifloxacin	Avelox
norfloxacin	Noroxin
ofloxacin	Floxin
gemifloxacin	Factive

References

1. IMS Health Vector One®, National Total Patient Tracker. Extracted July 2012
2. ICHARUS®. Extracted July 2012.